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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,499	12/03/2001	Malabika Ghosh	HYS-46	8107

7590

07/25/2003

Luisa Bigorina
HYSEQ, INC.
670 Almanor Avenue
Sunnyvale, CA 94085

EXAMINER

RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/005,499

Applicant(s)

GHOSH ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5 and 8-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5 and 8-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 5 and 8-11 are currently pending in this application.

Election/Restrictions

Applicant's election without traverse of Group II directed to the elected single polypeptide with SEQ ID NO: 378 in Paper No. 7 is acknowledged.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Objections

Claim 9 is objected to because of the following informalities: Claim 9 recites a grammatically improper phrase "comprising and amino acid sequence". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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Claims 5, 8, 9-11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The applicant has asserted utility for the polypeptide of SEQ ID NO:378 encoded by the isolated polynucleotide of SEQ ID NO:377 as having the properties of adiponectin (adiponectin-like) protein. However, the asserted utilities are not specific and substantial. While specification states that the protein of SEQ ID NO:378 is similar to adiponectin protein based on sequence similarity, the specification fails to assert such activity by an assay. Scientific literature recognizes a number of proteins as isolated from adipocytes. Even if one interpreted the disclosure as asserting that SEQ ID NO:378 is an adiponectin-like protein the art discloses a protein with 69.9% identity to SEQ ID NO:378 as a C1q-related factor expressed in the brain involved in motor function and another protein with 69.2% identity to SEQ ID NO:378 as a murine heat shock protein interacting protein HSP47, but not as having adiponectin-like properties (see enclosed sequence alignments with accession numbers O75973 and AAG64212). These proteins have substantially greater homology to the protein of SEQ ID NO:378 than any protein found in the prior art. As such a skilled artisan would not find an assertion that the protein of SEQ ID NO:378 is a adiponectin-like protein reasonable without further supporting evidence. No such evidence is presented in the specification. As adipocytes are known to produce a number of proteins with varied functions, a mere disclosure, that a protein is a adiponectin-like without a more specific recitation (type of activity supported by an assay) is insufficient to provide a substantial utility as the skilled artisan would require further research to identify or reasonably confirm a real world context of use.

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The specification also lists general use for the polypeptides as useful to treat “obesity, diabetes, lipoatrophy, coronary artery disease, atherosclerosis and other obesity and diabetes related disorders”. However, there is no information that links the use of the polypeptide of SEQ ID NO:378 or the polynucleotide of SEQ ID NO:377 encoding SEQ ID NO:378 and its variants to any specific disease state. Thus the asserted utility of the claimed polypeptides and its variants is not substantial or specific. For all the reasons detailed above, the claimed polypeptides lack, a specific, substantial and credible utility. Claims 5, 8, 9-11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with utility requirement of U.S.C. 101, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising or consisting of SEQ ID NO:378 and composition comprising the same, does not reasonably provide enablement for any polypeptide that is at least 99% identical to SEQ ID NO:378 or any polypeptide encoded by a polynucleotide that hybridizes to SEQ ID NO:377 under the conditions depicted in claim 10.

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The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 5, 10 and 11 are so broad as to encompass any polypeptide having 99% identity to SEQ ID NO: 378 or any polypeptide encoded by a polynucleotide that simply hybridizes to the polynucleotide with SEQ ID NO:377 under stringent conditions. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the polypeptide with SEQ ID NO:378. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides with an undefined function/activity. The specification is limited to teaching use of SEQ ID NO: 378 as a polypeptide having adiponectin-like but provides no guidance with regard to the making of

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variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polypeptide with 99% identity to SEQ ID NO:378 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting activity; (B) the general tolerance of the polypeptide with SEQ ID NO:378 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D)

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the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polypeptides with a number of amino acid modifications to SEQ ID NO:378. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 5, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5, 10 and 11 are directed to polypeptides that are 99% identical to SEQ ID NO:378 and polypeptides encoded by polynucleotides that hybridize to polynucleotide with SEQ ID NO:377 under stringent conditions. Claims 5, 10 and 11 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:378 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO:378 and fragments of SEQ ID NO:378 that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences or polypeptides encoded by polynucleotides that hybridize to polynucleotide with SEQ ID NO:377 under stringent conditions encompassed by the

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claim. No information, beyond the characterization of SEQ ID NO:378 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences encoded by polynucleotides that hybridize to polynucleotide with SEQ ID NO:377 under stringent conditions or polypeptides that are 99% identical to SEQ ID NO:378, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of functions. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Conclusion

None of the claims are allowable.

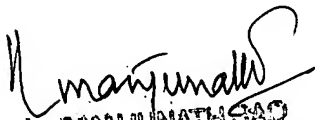
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is

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(703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao. Ph.D.
July 23, 2003